

WHAT IS CLAIMED IS:

- 1 1. A crystal of a core RNA polymerase (RNAP) that effectively diffracts X-rays  
2 for the determination of the atomic coordinates to a resolution of better than 3.5  
3 Angstroms.
- 1 2. The crystal of Claim 1, wherein the core RNA polymerase is a bacterial core  
2 RNA polymerase.
- 1 3. The crystal of Claim 2, wherein the bacterial core RNA polymerase is a  
2 thermophilic bacterial core RNA polymerase.
- 1 4. The crystal of Claim 3, wherein the thermophilic bacterial core RNA  
2 polymerase is a *Thermus aquaticus* bacterial core RNA polymerase.
- 1 5. The crystal of Claim 1, wherein the core RNA polymerase comprises a  $\beta'$   
2 subunit, a  $\beta$  subunit, and a pair of  $\alpha$  subunits.
- 1 6. The crystal of Claim 5, further comprising an  $\omega$  subunit.
- 1 7. The crystal of Claim 1 that effectively diffracts X-rays for the determination  
2 of the atomic coordinates of the core RNA polymerase to a resolution of 3.3  
3 Angstroms or better.
- 1 8. The crystal of Claim 7 having space group of  $P4_12_12$  and a unit cell of  
2 dimensions of  $a = b = 201$  and  $c = 294 \text{ \AA}$ .
- 1 9. A method of identifying an agent for use as an inhibitor of bacterial RNA  
2 polymerase using the crystal of Claim 1 or a dataset comprising the three-  
3 dimensional coordinates obtained from the crystal, comprising:

4 (a) selecting a potential agent by performing rational drug design with  
5 the three-dimensional coordinates determined from the crystal, wherein said  
6 selecting is performed in conjunction with computer modeling;

7 (b) contacting the potential agent with the bacterial RNA polymerase;  
8 and

9 (c) measuring the activity of the bacterial RNA polymerase; wherein a  
10 potential agent is identified as an agent that inhibits bacterial RNA polymerase when  
11 there is a decrease in the activity of the bacterial RNA polymerase.

1 10. The method of Claim 9, further comprising:

2 (d) growing a supplemental crystal containing the core RNA polymerase  
3 formed in the presence of the potential agent, wherein the crystal effectively  
4 diffracts X-rays for the determination of the atomic coordinates to a resolution of  
5 better than 5.0 Angstroms;

6 (e) determining the three-dimensional coordinates of the supplemental  
7 crystal with molecular replacement analysis; and

8 (f) selecting a second generation agent by performing rational drug  
9 design with the three-dimensional coordinates determined for the supplemental  
10 crystal, wherein said selecting is performed in conjunction with computer modeling.

1 11. The method of Claim 10, further comprising:

2 (g) contacting the second generation agent with a eukaryotic RNA  
3 polymerase; and

4 (h) measuring the activity of the eukaryotic RNA polymerase; wherein a  
5 potential agent is identified as an agent for use as an inhibitor of bacterial RNA  
6 polymerase when there is no change in the activity of the eukaryotic agent RNA  
7 polymerase.

1 12. A method of identifying an agent that inhibits bacterial growth using the  
2 crystal of Claim 1, or a dataset comprising the three-dimensional coordinates  
3 obtained from the crystal, comprising:  
4 (a) selecting a potential agent by performing rational drug design with  
5 the three-dimensional coordinates determined for the crystal, wherein said selecting  
6 is performed in conjunction with computer modeling;  
7 (b) contacting the potential agent with a bacterial culture; and  
8 (c) measuring the growth of the bacterial culture; wherein a potential  
9 agent is identified as an agent that inhibits bacterial growth when there is a decrease  
10 in the growth of the bacterial culture.

1 13. The method of Claim 12, further comprising:  
2 (d) growing a supplemental crystal containing the core RNA polymerase  
3 formed in the presence of the potential agent, wherein the crystal effectively  
4 diffracts X-rays for the determination of the atomic coordinates to a resolution of  
5 better than 5.0 Angstroms;  
6 (e) determining the three-dimensional coordinates of the supplemental  
7 crystal with molecular replacement analysis; and  
8 (f) selecting a second generation agent by performing rational drug  
9 design with the three-dimensional coordinates determined for the supplemental  
10 crystal, wherein said selecting is performed in conjunction with computer modeling.

1 14. The method of Claim 13, further comprising:  
2 (g) contacting the second generation agent with a eukaryotic cell; and  
3 (h) measuring the amount of proliferation of the eukaryotic cell; wherein  
4 a potential agent is identified as an agent for inhibiting bacterial growth when there  
5 is no change in the proliferation of the eukaryotic cell.

1 15. A method of identifying an agent for use as an inhibitor of bacterial RNA  
2 polymerase using the three-dimensional coordinates for the *Thermus aquaticus* core  
3 RNA polymerase comprising:

4 (a) selecting a potential agent by performing rational drug design with  
5 the three-dimensional coordinates determined for the *Thermus aquaticus* core RNA  
6 polymerase, wherein said selecting is performed in conjunction with computer  
7 modeling;

8 (b) contacting the potential agent with the bacterial RNA polymerase;  
9 and

10 (c) measuring the activity of the bacterial RNA polymerase; wherein a  
11 potential agent is identified as an agent that inhibits bacterial RNA polymerase when  
12 there is a decrease in the activity of the bacterial RNA polymerase.

1 16. The method of Claim 15, further comprising:

2 (d) growing a crystal containing a bacterial RNA polymerase formed in  
3 the presence of the potential agent, wherein the crystal effectively diffracts X-rays  
4 for the determination of the atomic coordinates to a resolution of better than 5.0  
5 Angstroms;

6 (e) determining the three-dimensional coordinates of the crystal with  
7 molecular replacement analysis; and

8 (f) selecting a second generation agent by performing rational drug  
9 design with the three-dimensional coordinates determined for the crystal, wherein  
10 said selecting is performed in conjunction with computer modeling.

1 17. The method of Claim 16, further comprising:

2 (g) contacting the second generation agent with a eukaryotic RNA  
3 polymerase; and

4 (h) measuring the activity of the eukaryotic RNA polymerase; wherein a  
5 potential agent is identified as an agent for use as an inhibitor of bacterial RNA

6 polymerase when there is no change in the activity of the eukaryotic agent RNA  
7 polymerase.

1 18. A method of identifying an agent that inhibits bacterial growth using the  
2 three-dimensional coordinates obtained for the *Thermus aquaticus* core RNA  
3 polymerase, comprising:

4 (a) selecting a potential agent by performing rational drug design with  
5 the three-dimensional coordinates determined for the *Thermus aquaticus* core RNA  
6 polymerase, wherein said selecting is performed in conjunction with computer  
7 modeling;

8 (b) contacting the potential agent with a bacterial culture; and

9 (c) measuring the growth of the bacterial culture; wherein a potential  
10 agent is identified as an agent that inhibits bacterial growth when there is a decrease  
11 in the growth of the bacterial culture.

1 19. The method of Claim 18 further comprising:

2 (d) growing a crystal containing a bacterial RNA polymerase formed in  
3 the presence of the potential agent, wherein the crystal effectively diffracts X-rays  
4 for the determination of the atomic coordinates to a resolution of better than 5.0  
5 Angstroms;

6 (e) determining the three-dimensional coordinates of the crystal with  
7 molecular replacement analysis; and

8 (f) selecting a second generation agent by performing rational drug  
9 design with the three-dimensional coordinates determined for the crystal, wherein  
10 said selecting is performed in conjunction with computer modeling.

1 20. The method of Claim 19, further comprising:

2 (g) contacting the second generation agent with a eukaryotic cell; and

3 (h) measuring the amount of proliferation of the eukaryotic cell; wherein  
4 a potential agent is identified as an agent for inhibiting bacterial growth when there  
5 is no change in the proliferation of the eukaryotic cell.

1 21. A method of obtaining a crystal of a core bacterial RNA polymerase  
2 comprising growing a core bacterial RNA polymerase crystal in a buffered solution  
3 containing 40-45% saturated ammonium sulfate.

1 22. The method of Claim 21 wherein said growing is performed by a method  
2 selected from the group consisting of batch crystallization, vapor diffusion, and  
3 microdialysis.

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